Claim 41 (added) A pharmaceutical composition comprising one or more primary aliphatic alcohol fatty acid esters of Claim 1, in combination with a pharmaceutically acceptable carrier, excipient, or dilutant.

Claim 42 (added) The composition according to Claim 5 in the form of a capsule, tablet, liquid or powder.

Claim 43 (added) A method for lowering serum cholesterol levels in human subjects, which comprises orally administering to the human subjects an effective amount of the composition according to Claim 4.

Claim 44 (added) A method for lowering serum cholesterol in human subjects, which comprises orally administering to the human subjects a pharmaceutically effective amount of the composition according to Claim 5.

REMARKS:

The Examiner's Office Action has been reviewed and considered, and revised claims are submitted in light of the Examiner's comments.

Applicant has amended Claims 1-5, deleted Claim 36, and has added new Claims 37- 44. In view of the amendments and the remarks below, Applicant respectfully submits that the cited references do not singularly or in combination anticipate, teach, or suggest the inventions that are the subject of the amended and newly submitted claims.

Anticipation

As stated by the Examiner, Levin et al. discloses compositions containing esters of tetracosanol, hexacosanol, octacosanol, and triacontanol, where the acid residue may be organic or inorganic acid. Levin et al. discloses the use of these esters for reducing anoxia, for

improving physical endurance, or for improving heart response. Levin discloses that suitable organic acid radicals include phenoxyacetic acid, benzoic acid, 2 to 3 carbon atom fatty acids like acetic acid and propionic acid, and dicarboxilic acids like succinic or phtalic acid.

Applicant claims a novel composition of policosanol esters. Applicant's Claim 1 has been amended to be limited to fatty acids of long chain carbon atoms. Levin et al. specifically limits its disclosure and embodiments to short chain (i.e. *2 to 3* carbon atom) fatty acids and does not mention or disclose the possibility of other suitable fatty acids. The mere mention of "organic acid" is not tantamount to disclosing every possible organic acid, as the number and variety of such are extensive. Applicant respectfully disagrees with Examiner's statement that esters of policosanols are considered to be a genus. Applicant instead states that esters of policosanols of organic acids constitute a wide array of different organic compounds. By limiting amended Claim 1 to policosanol esters of fatty acids where the fatty acid residue has a long chain of carbon atoms, Applicant is claiming a novel composition of policosanol esters not anticipated by Levin et al.

Obviousness

The following comments address the four references the examiner relied upon in raising a case of *prima facie* obviousness.

U.S. Patent No. 3,031,376, Levin et al. teaches that policosanol fatty acid esters, where fatty acids contain 2 to 3 carbon atoms, are useful for reducing anoxia or stimulating heart response and does not at all relate to or teach the utilization of policosanol fatty acid esters with 2 to 3 carbon atoms to treat hypercholesterolemia. Clearly this reference is inapplicable prior art

because it does not address the objective of using policosanol fatty acid esters, particularly those with a long chain of carbon atoms, for the purpose of treating hypercholesterolemia.

On the other hand, U.S. Patent No. 5,663,156, Granja et al. discloses that policosanols such as tetracosanol, hexacosanol, heptacosanol, and traicontanol are useful in compositions and methods for treating hypercholesterolemia and atherosclerosis. However, Granja et al. actually teaches away from the use of fatty acid esters of policosanols for the treatment of hypercholesterolemia. Granja et al. teaches hydrolizing the esters, ***discarding*** the fatty acid residue, and using the free policosanol mixture. Nowhere does Granja et al. suggest the use of the waxes (policosanol esters with long chain fatty acids) instead of the free policosanols for the use as cholesterol-lowering agents. Thus, Granja et al. is inapplicable prior art in that it teaches away the use of fatty acids together with policosanols by specifically claiming the discarding of fatty acid moiety of waxes.

Hasegawa (Chem. Abst. 100:208354) teaches that compositions containing linoleic acids are useful for treating hypercholesterolemia. However, there is no basis to then *a priori* conclude that a policosanol fatty acid ester will also yield a useful result in treating hypercholesterolemia. In fact, there is no basis to *a priori* conclude that the above combination will yield a *synergistic* or *superior* effect compared to when they are used individually. More specifically, merely because octacosanol and lineoic acid are each effective at treating hypercholesterolemia does not mean that octacosanyl linoleato is as effective or more effective at treating the same. There is no routine belief that where drug A and drug B are separately and individually useful in treating a certain condition, that the combination of these two will

necessarily yield superior results. On the contrary, in view of Bundgaard, the assumption would be that no synergy would result.

The Bundgaard reference teaches that esters of active drug substances are hydrolyzed within the body (in vivo) by cleaving the ester bond to regenerate the active drug substance. Bungaard teaches away the combination (policosanol fatty acid ester) because it teaches that the ester compound will be split within the body into single ester compounds, letting each moiety act independently.

For a rejection to be proper, the claimed invention as a whole of the rejected claim must have been obvious under §103. Although it is common to find features in the prior art, it is not isolated features but the subject matter as a whole that must be evaluated under 35 U.S.C. § 103. There are significant differences between the claimed invention and the prior art references that must be considered.

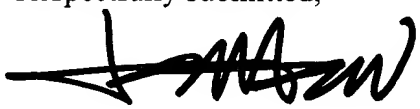
All of the prior art quoted by the Examiner lack significant features and are too remote from one another to be combined to conclude *prima facie* obviousness. Levin et al. discloses the use of policosanol fatty acid esters specifically with short chain carbon atoms to treat anoxia or heart response problems – in no way does it reveal the use of policosanol fatty acid esters to treat hypercholesterolemia, particularly where the fatty acid are of long chain carbon atoms. Granja et al. teaches simply the use of policosanols, while Hasegawa teaches simply the use of linoleic acids for treating hypercholesterolemia – nowhere do either reveal or imply that the combination of the two compounds would improve treatment of hypercholesterolemia. In fact, Granja et al. actually teaches away the use of fatty acid esters of policosanol. Finally Bundgaard teaches away the use of the combination of policosanols and linoleic acid by revealing that the

synthesized ester compound would be split in vivo, leaving each component to act independently. There is no discovery of synergy or superior functionality as is claimed by the Applicant's invention, whose conclusion was derived through multiple trials and significant research.

It is Applicant's belief that this application is in a condition for allowance. An action so indicating is respectfully requested. If the Examiner believes that discussion of this application would be beneficial, the undersigned may be contacted at the telephone number stated below.

November 18, 2003

Respectfully submitted,



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